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Ureteroscopic lithotripsy for ureteral stones in children using holmium: yag laser energy: results of a multicentric survey

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Summary

Background
Holmium:YAG (Ho:YAG) laser lithotripsy has broadened the indications for ureteroscopic stone managements in adults, but few evidence are currently available in the pediatric population.

Objective
This article aimed to assess the outcome of Ho:YAG laser lithotripsy during retrograde ureteroscopic management of ureteral stones in different locations in children.

Study design
The medical records of 149 patients (71 boys and 78 girls; median age 9.2 years) treated with Ho:YAG laser ureteroscopic lithotripsy in five international pediatric urology units over the last 5 years were retrospectively reviewed. Exclusion criteria included patients with renal calculi and/or with a history of ipsilateral stricture, renal failure, active urinary tract infection, or coagulation disorder.

Results
Stones were treated with dusting technique in all cases. The median stone size was 10.3 mm (range 5–17). Stones were located in the distal ureter in 77 cases (51.7%), in the middle ureter in 23 cases (15.4%), and in the proximal ureter in 49 cases (32.9%). The median operative time was 29.8 min (range 20–95). Intra-operative complications included five bleedings (3.3%) and seven stone retropulsions (4.7%). Overall stone-free rate was 97.3%. Overall postoperative complications rate was 4.0% and included two cases of stent migration (1.3%) (Clavien II) and four residual stone fragments (2.7%) that were successfully treated using the same technique (Clavien IIIb). On multivariate analysis, re-operation rate was significantly dependent on the proximal stone location and presence of residual fragments >2 mm ($P = 0.001$).

Discussion
This study is one of the largest pediatric series among those published until now. The study series reported a shorter operative time, a higher success rate, and a lower postoperative complications rate compared with previous series. A limitation of this study is that stone-free rates may be somewhat inaccurate using ultrasonography and plain X-ray compared with computed tomography (CT); the study's 97.3% success rate may be overestimated because no CT scan was done postoperatively to check the stone-free rate. Other limitations of this article include its retrospective nature, the multi-institutional participation, and the heterogeneous patient collective.

Conclusion
The Ho:YAG laser ureteroscopic lithotripsy seems to be an excellent first-line treatment for children with ureteral stones, independently from primary location and size. However, patients with proximal ureteral stones and residual fragments >2 mm reported a higher risk to require a secondary procedure to become stone-free. Combination of techniques as well as appropriate endourologic tools are key points for the success of the procedure regardless of stones' size and location.

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Introduction

The prevalence of urolithiasis is increasing worldwide and is causing significant morbidity and cost to the healthcare systems [1]. While minimally invasive therapies remain the mainstay of treatment, there has been a notable increase in the use of ureteroscopy (URS), so that URS is now the most common surgical therapy for upper urinary tract stones in North America [2]. One reason for the shift in practice toward URS has been the widespread availability of the holmium laser, which permits lithotripsy in all stone locations, regardless of stone composition [3].

Holmium:YAG (Ho:YAG) laser lithotripsy has broadened the indications for ureteroscopic stone managements in adults, but few evidence are currently available in the pediatric population. Ureteral calculi in children are less frequent than in adults, representing only about 7% of total urinary calculi but are usually a challenge to the urologist [4]. In the absence of indications for intervention, pediatric ureteral stones <3 mm are likely to be passed spontaneously, but stones >4 mm in the distal ureter are likely to require endourologic treatment [5]. In general, the surgical strategy for treating upper urinary tract stones with URS consists of either fragmentation and active basket retrieval or fragmentation resulting in fine fragments left in situ for spontaneous passage, also known as dusting technique [6]. The standard preference in ureteroscopic lithotripsy is use of Ho:YAG laser, which can effectively break stones into fragments small enough to remove or pass spontaneously. The mode of fragmentation employed to clear stones during ureteroscopic laser lithotripsy raises concerns related to operative time, associated morbidity and costs, and especially potential endoscope damage. There is no consensus on how to achieve optimal stone clearance once the primary stone has been fragmented with lithotripsy. However, the dusting technique can theoretically decrease operative times and lower the risk of ureteral trauma by minimizing the repetitive introduction and removal of the ureteroscope [7]. There is a growing body of literature that supports this treatment modality in children with minimal morbidity [8,9]. However, reports of ureteroscopic laser lithotripsy are not as common in prepubertal patients. In addition, little is known about the success of URS for proximal stones, especially in the era of Ho:YAG laser lithotripsy [10].

This multicentric study aimed to assess the efficacy and safety of Ho:YAG laser lithotripsy during retrograde ureteroscopic management of ureteral stones in different locations in children.

Patients and methods

The medical records of 149 patients (71 boys and 78 girls) treated with Ho:YAG laser ureteroscopic lithotripsy in five international pediatric urology units over the last 5 years were retrospectively reviewed.

Exclusion criteria included patients with renal calculi and/or with a history of ipsilateral stricture, renal failure, active UTI, or coagulation disorder. The most common presentation symptoms were colicky pain and vomiting, occurring in 81.9% of cases, followed by gross hematuria in 10.1% and UTIs in 8%. Pre-operative diagnosis included clinical evaluation, urine analysis with additional urine culture if there was suspicion of a UTI, measurement of serum creatinine, a plain abdominal X-ray and abdominal ultrasonography (US) in all patients. Non-contrast computerized tomography (NCCT) was performed, when available. The diagnosis of impacted stones in patients who had not undergone NCCT pre-operatively was confirmed via preoperative retrograde ureterography and/or ureteroscopic visualization under direct vision.

The operative time was calculated from the time when the patient was positioned for the surgery to when the drapes were taken off. All the procedures were performed by a single expert surgeon in each participating center. Each expert surgeon had more than 10 years of experience in endoscopic surgery and performed over 100 endoscopic urological procedures per year and at least 10–15 ureteroscopic procedures per year. The hospital stay length included only the purely hospital admission time specific to surgical procedure, whereas the time in hospital for the patients admitted with symptomatic renal colic and subsequently operated on was excluded. Postoperatively, all patients were prescribed Mg K citratum to prevent stone recurrence. Follow-up consisted of renal tract US and plain abdominal X-ray 1, 3, 6, and 12 months after the procedure and thereafter once a year to rule out obstruction or clinically significant renal fragments (>2 mm). No computed tomography (CT) scan was done postoperatively to check stone-free rate. Assessment of the procedure outcomes included stone-free and complications rates. The authors defined as 'stone-free' patients with complete clearance of stones or at least residual fragments <2 mm in urinary system on the postoperative imaging at least after 1 month to allow the ureter to recover from any postoperative edema as a result of ureteroscopic manipulation and fragmentation and give enough time for any fragments to clear spontaneously. Complications were classified according to the Clavien-Dindo grading system [11].

The authors performed a multivariate logistic regression analysis to assess risk factors for re-operation. Factors assessed included patients' age, patients' weight, proximal stone location, distal stone location, stone size, residual fragments size, operative time, and degree of hydronephrosis. Significance was considered as P-value <0.05. Statistical analysis was done using the computer software SPSS 17.0 for Windows XP.

The study received the appropriate institution review board approval.

Surgical technique

All the procedures were performed under general anesthesia. Patients were placed in the lithotomy position on the operative table. Routine prophylactic antibiotics were administered. Fluoroscopic monitoring was available. All patients underwent initial cystoscopy to place a safety or working guidewire into the proximal ureter or collecting system. Ureteroscopy was performed using a 4.5 or 7.5 or 9 Fr semi-rigid ureteroscope, according to the patient's age, with no need for prestenting in any patients. A safety guidewire was used in all cases. A flexible ureteroscope was adopted only in cases of stone retropulsion to pelvis lower pole. An active dilatation of the uretero-vesical junction using ureteral access sheaths was performed in only five cases of the study series (3.3%). The authors recommend the use of ureteral access sheaths when the ureter is not appropriately capacious to allow an easy introduction of the ureteroscope to facilitate repeated upper tract access, reduce intrarenal pressures, and decrease operative time.

Stones were treated with the dusting technique in all cases (Fig. 1). The Ho:YAG laser was set-up at a pulse energy of 0.5 J and a frequency of 20 Hz or higher. Laser fibers with a diameter ranging from 272 to 365 micron were adopted in accordance to the type of ureteroscope used, flexible or semi-rigid, respectively. The stones were fragmented until they were deemed small enough to pass spontaneously in most of the study cases (Video 1). Only in few cases, fragments of stones were persistent despite laser application using dusting settings and were removed by using a stone basket or a grasper to achieve samples for stone composition analysis. In cases of retropulsed stones, they were treated using non-contact laser lithotripsy. In this technique, stone fragments are pulverized in a calyx with the laser fibers activated in bursts, away from the stone fragments resulting in a whirlpool-like effect that causes stones to collide and fragment further to produce fine stone residue for spontaneous passage. It is also commonly known as the 'popcorn' effect [6]. A ureteral JJ stent was routinely indwelled and removed at mean 3 weeks postoperatively under short-duration anesthesia in all patients. A bladder catheter was placed for at least 12 h postoperatively in all patients.

Supplementary video related to this article can be found at https://doi.org/10.1016/j.jpurol.2019.05.004

The following is the supplementary data related to this article:

Results

The median patients' age was 9.2 years (range 1—18), and their median weight was 36.8 Kgs (range 13—78). Associated pathologies included meningomyelocele (n = 3), cystinuria (n = 2), cystic fibrosis (n = 1), muscular dystrophy (n = 1), horse-shoe kidney (n = 1), and solitary kidney (n = 1). The median stone size was 10.3 mm (range 5—17). Stones were located in the distal ureter in 77 cases (51.7%), in the middle ureter in 23 (15.4%), and in the proximal ureter in 49 (32.9%). Pre-operative hydronephrosis on the affected side (median 14.8 mm) with a dilatation of the ureter above the stone was diagnosed with US in all patients.

The median operative time was 29.8 min (range 20—95). Intra-operative complications included five bleedings (3.3%) and seven stone retropulsions (4.7%). Stone migration upward into the kidney during laser lithotripsy occurred in patients with proximal ureteral stones associated with severe hydroureteronephrosis. These cases were treated using flexible ureteroscope. The median analgesic requirement (paracetamol, tramadol) was 16.7 h (range 3—72). The median hospital stay was 1.2 days (range 1—3). The median follow-up length was 26.4 months (range 3—69). Overall stone-free rate was 97.3%. The median number of procedures needed for obtaining stone-free ureters was 0.9 $\pm$ 0.5. Overall postoperative complications rate was 4.0% and included two cases of stent migration (1.3%) (Clavien II) and four cases with residual stone fragments (2.7%) that were successfully treated using the same technique (Clavien IIIb).

No laser-induced complications were noticed. Stone analysis was available from 74 patients (49.6%) and revealed a composition of calcium oxalate in 66.2%, cysteine in 20.3%, struvite in 9.4%, and uric acid in 4.1%. Fifty-five out of 74 patients (74.3%) had identifiable metabolic abnormalities; the most common finding was hypocitraturia, followed by hypercalciuria. No influence of stone composition on laser efficacy, operative time, or complications rates was demonstrated in the study series.

All patients' demographics and outcome parameters are reported in Table 1.

On multivariate analysis, proximal stone location and residual fragments >2 mm were associated with higher rates of re-operation ($P = 0.001$) (Table 2). Regarding patients' age, 32 patients (21.4%) were aged less than 5 years, and the authors reported one intra-operative bleeding and one postoperative stent migration in this younger patients' group, with no significant difference in complications rate compared with the older patients' group ($P = 0.55$).

Discussion

Urinary stone disease is becoming a more important health problem in the pediatric population because of the increasing incidence of urolithiasis [1,12]. The use of URS in children has been limited in Europe because of concerns regarding the risk of ureteral ischemia, perforation, stricture formation, and development of vesicoureteral reflux

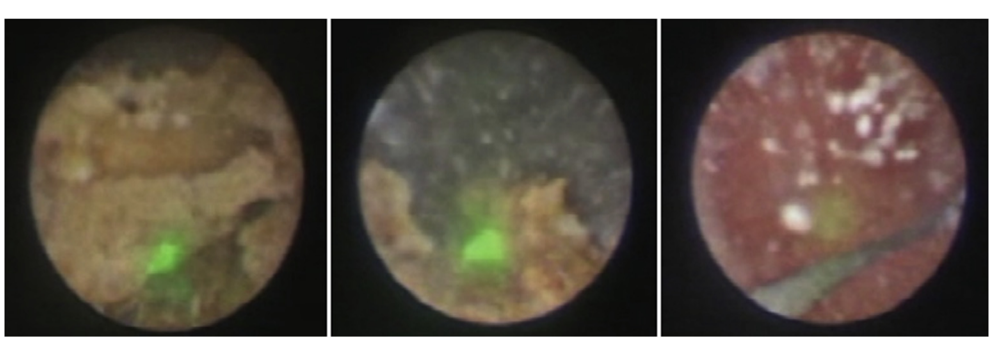

Fig. 1 In the dusting technique, the stone fragments are pulverized to allow spontaneous passage.

Table 1 Patients' demographics and outcome parameters in the study series.

Patients' demographics	
Male patients, n (%)	71 (47.6%)
Female patients, n (%)	78 (52.4%)
Median age, years [range]	9.2 [1–18]
Median weight, Kgs [range]	36.8 [13–78]
Associated pathologies, n (%)	
Meningomyelocele	3 (2.0%)
Cystinuria	2 (1.3%)
Cystic fibrosis	1 (0.65%)
Muscular dystrophy	1 (0.65%)
Horse-shoe kidney	1 (0.65%)
Solitary kidney	1 (0.65%)
Symptoms, n (%)	
Colicky pain	122 (81.9%)
Vomiting	122 (81.9%)
Hematuria	15 (10.1%)
Urinary tract infections	12 (8.0%)
Median stone size, mm [range]	10.3 [5–17]
Stones location, n (%)	
Distal ureter	77 (51.7%)
Middle ureter	23 (15.4%)
Proximal ureter	49 (32.9%)
Outcome parameters	
Median operative time, minutes [range]	29.8 [20–95]
Median analgesic requirement, hours [range]	16.7 [3–72]
Median hospital stay, days [range]	1.2 [1–3]
Intra-operative complications, n (%)	
Bleeding	5 (3.3%)
Stone retropulsion	7 (4.7%)
Overall stone-free rate	145 (97.3%)
Median number of procedures for obtaining stone-free ureters	0.9 $\pm$ 0.5
Postoperative complications, n (%)	
Stent migration	2 (1.3%) – Clavien II
Residual stone fragments	4 (2.7%) – Clavien IIIb
Stone analysis results, n (%)	74 (49.6%)
Calcium oxalate	49 (66.2%)
Cysteine	15 (20.3%)
Struvite	7 (9.4%)
Uric acid	3 (4.1%)

Table 2 Multivariate logistic regression analysis of demographics and operative factors associated with re-operation in the study series.

Variable	OR	95% CI	*P*-value
Patients' age (years)	0.934	0.557–1.566	0.795
Patients' weight (Kgs)	0.955	0.598–1.578	0.813
Proximal stone location	1.008	1.001–1.029	0.001
Distal stone location	0.985	0.648–1.498	0.943
Stone size (mm)	0.895	0.547–1.398	0.856
Residual fragments size (mm)	1.015	1.005–1.036	0.001
Operative time (minutes)	0.944	0.575–1.767	0.782
Degree of hydronephrosis (mm)	0.755	0.456–1.285	0.873

OR, odds ratio; CI, confidence interval.

of small caliber ureteral orifices, whereas it has been the standard of care in the United States for 10–15 years at least [13]. Recently, the advent of minimally invasive techniques has dramatically changed the approach to several pediatric urological pathologies worldwide [14,15]. With the downsizing of ureteroscopes and miniaturization of working instruments and intracorporeal lithotripsy devices, URS has become a more attractive therapeutic option for pediatric ureteral stones [16]. With the introduction of the Ho:YAG laser, the efficacy of ureteroscopic lithotripsy has been much improved. The technique is easy and has a short learning curve. The increased costs of the device and the fibers and the prolonged time needed for the lithotripsy process have been cited as the main disadvantages of the Ho:YAG laser [8]. However, considering its versatility, this device may in fact become cost-effective. The holmium laser is widely used in endourology practice because of the minimal thermal injury related to laser ablation and its success in fragmenting all stone components [17]. In addition, holmium lasers can vaporize soft tissues and cause coagulation, and they have excellent cutting ability. Moreover, they have a limited tissue penetration of 0.5 mm, which makes them one of the safest types of lithotripters. These properties make the holmium laser a very good instrument for the treatment of every type of ureteral stones, regardless of their location and composition.

There is much controversy regarding the best Ho:YAG laser energy setting to fragment urinary stones. Some authors favor stone fragmentation entirely to dust leaving no fragments to remove afterward, with the intention that achieving such a small stone size will allow the stones to pass spontaneously. Others prefer fragmentation into extractable pieces, which can result in many trips through the ureter to retrieve stone fragments [7]. It is known that the mode of fragmentation has an impact on the fragmentation time, operative time, stone-free rate, complications rate, and stone retropulsion [18]. In a recent study by Fahmy et al. [7], the authors stated that stone dusting was associated with a significantly longer fragmentation time and operative time than fragmentation into extractable pieces.

The authors analyzed the current literature focused on management of ureteral stones with laser ureteroscopic lithotripsy [7,10,13,19–25], and the authors found that this study is one of the largest pediatric series among those published until now. An interesting finding is that the study series reported a shorter operative time compared with that of the previous series ranging between 32 and 77 min (Table 3). Probably, this result is related to the learning curve and single-surgeon's experience with the technique. Each surgeon's expertise was defined on the basis of both his volume of activity and his years of experience with the technique. In fact, each participating surgeon was considered expert if he had more than 10 years of experience in endoscopic surgery and performed over 100 endoscopic urological procedures per year and at least 10–15 ureteroscopic procedures per year.

In the current study, the authors also attempted to fill the gap in the understanding of the factors associated with

Table 3 Outcome analysis of published series on laser ureteroscopic lithotripsy in children.

Reference	Number of patients	Average operative time (minutes)	Overall stone-free rate	Intra-operative stone retropulsion rate	Other intra-operative complications rate	Overall postoperative complications rate
Fahmy et al 2016[7]	100	32	98%	3%	0	8%
Elsheemy et al 2014[19]	104	45	81.25%	4.7%	14%	18.75%
Galaletal 2013[20]	18	NR	89%	5.5%	5.5%	27.7%
Tiryaki et al 2013[21]	32	NR	92.68%	0	7.3%	2.4%
Yucel et al 2011[22]	48	77	84.3%	0	0	14.8%
Turunc et al 2010[23]	61	NR	84.8%	NR	NR	NR
Ozkan et al 2010[24]	26	NR	84.6%	0	0	46%
Erturhan et al 2007[25]	41	NR	87.8%	4.8%	7%	4.8%
Thomas et al 2005[13]	29	NR	88%	3.4%	3.4%	0
Lam et al 2002[10]	67	41.4	96.5%	0	0	0

NR, not reported.

the risk of re-operation. To date, no studies focused on this topic exist in the current pediatric literature. This study is probably the first to demonstrate a significant association between proximal stone location and residual fragments >2 mm and risk of re-operation. These findings suggest the importance to obtain the complete clearance of stones during ureteroscopic procedures by adopting preferentially the dusting technique that allows to pulverize the stones or alternatively the fragmentation technique with extraction of all fragments. The authors believe that the choice of the best setting between dusting and fragmentation or a combination of both remains one of surgeon preference and should be tailored to an individual basis.

In common practice, the authors prefer to use dusting technique because it theoretically decreases operative time and the risk of ureteral trauma related to multiple passes of the ureteroscope and eliminates the need for a stone extraction device. However, potential risks have been reported with the dusting technique, such as stone recurrence from fragments failing to pass. In the authors experience, if fragments of stones were persistent despite laser application using dusting settings, the authors extracted them using a grasper or a basket with no increase of operative time or intra-operative complications. In cases with difficult ureteral access to proximal ureteral stones, the authors recommend the use of ureteral access sheaths to facilitate repeated upper tract access, reduce intrarenal pressures, and decrease operative time. An intra-operative challenge is also represented by stone retropulsion because it reduces the laser's efficiency, prolongs the operative time, and sometimes makes the stone inaccessible [26]. Several studies have concluded that setting of the Ho:YAG laser with lower pulse energy and higher pulse rates would minimize such complications [16,27]. In the study series, the authors always used the same laser setting with a pulse energy of 0.5 J and a frequency of 20 Hz or higher, and the authors reported a 4.7% stone retropulsion rate, that was consistent with most reports in the literature (Table 3). In the authors experience, all stone migrations occurred in cases with proximal ureteral stones associated with severe hydroureteronephrosis and were solved intra-operatively using a flexible ureteroscope. The retropulsed stones in the lower calyx were dusted using the 'popcorn technique' [6]. In some cases, stone retropulsion may also result advantageous to address some mid or proximal stones within the renal collecting system to avoid ureteral wall damage [26].

The Ho:YAG laser ureteroscopic lithotripsy reported a high success rate, with an overall stone free rate of 97.3% in the study series, that was higher than that reported in most of the previously published series (Table 3). However, the 97.3% success rate may be overestimated because no CT scan was done postoperatively to check the stone-free rate in the study series. A limitation of this study is that stone-free rates and stone sizes may be somewhat inaccurate using US and plain X-ray compared with CT. In fact, the operator-dependent nature of US can miss stone fragments <2 mm, whereas the plain X-ray cannot detect radiolucent stones obscured by overlying bowel gas or stool. The authors preferred to not routinely perform CT scans during follow-up to avoid the higher radiation exposure compared with US and X-ray and the need for sedation in not collaborative patients. The authors decided to apply the following follow-up protocol: renal tract US and plain abdominal X-ray 1, 3, 6, and 12 months after the procedure and thereafter once a year to rule out obstruction or clinically significant stone fragments (>2 mm). The authors defined as 'stone-free' patients with complete clearance of stones or at least residual fragments <2 mm in urinary system on the postoperative imaging. In a recent paper by Iremashvili et al. [28], it was demonstrated that non-obese patients with residual stone fragments of any size are at increased risk for repeat intervention compared with those with a negative abdominal X-ray. Despite the evidence reported in the paper by Iremashvili et al. [28], all patients of the study series, who underwent repeat surgery, presented stone fragments >2 mm. Consequently, despite the limited accuracy to detect small stone fragments, abdominal X-ray can be endorsed as an acceptable method of postoperative imaging after URS, considering that in the authors experience, only patients with residual fragments greater than 2 mm required re-operation.

Other limitations of this paper include the retrospective nature of the study, that may cause a deficiency in the recording of complications, the multi-institutional participation and the heterogeneous patient collective, that made the data hardly comparable, and the follow-up periods that were not long enough to confirm the safety of the procedure.

Overall postoperative complications rate (4%) and reoperation rate (2.7%) reported in the study series were lower compared with most previous series (Table 3). A recent paper reported that several factors including younger age (<2 years), upper ureteric stones, smaller ureters, and larger stones (>15 mm) were associated with increased complications and failure rates of laser lithotripsy [19]. Another paper concluded that the stone localization and stone size are the factors that significantly affect the success of the procedure [23]. The authors also analyzed the impact of various factors including patients' age, patients' weight, proximal stone location, distal stone location, stone size, residual fragments size, operative time, and degree of hydronephrosis on the outcome of the procedure. On multivariate analysis, proximal stone location and presence of residual fragments greater than 2 mm were associated with higher rates of reoperation in the study series.

It is also known that laser settings for dusting seem to be most effective for stones under 1100 Hounsfield Unit (HU), such as calcium oxalate dihydrate, uric acid, or calcium phosphate. Dusting technique may lose its efficacy with denser stones (>1100 HU), such as calcium oxalate monohydrate or cysteine, which are typically harder and tend to fragment into large pieces that may require use of a retrieval device [6]. No influence of stone composition on laser efficacy, operative time, or complications rates was demonstrated in the study series. The reason was probably related to the more powerful Ho-YAG laser generator, that the authors currently adopt, which allows higher frequency settings up to 80 Hz. Such versatility in laser parameters may allow a similar good outcome with various stone types and locations, as reported in the study series.

In conclusion, the Ho:YAG laser ureteroscopic lithotripsy, performed by skilled and experienced hands, had high success rates, low retreatment requirements, and acceptable complications rates, thus making it a safe and effective first-choice treatment for ureteral stones in children, in whom conservative therapy fails. Overall stone-free rate was very high in the study series (97.3%). Patients with stones located in the proximal ureter and residual fragments greater than 2 mm reported a higher risk to require a secondary procedure to become stone-free. The surgeons should be aware of the current equipment available to facilitate pediatric endoscopy and master all available treatment options to personalize care. The authors believe that an optimal approach may be some combination of the techniques based on numerous stone factors including size, location, and density as well as each patient's anatomic features.

Author statements

Ethical approval

The work has received ethical approval.

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Competing interest

None.

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